UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,049	07/15/2003	Barrett R. Harvey	UTSB:721US	8228

32425 7590 06/24/2004

FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,049	HARVEY	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- *If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.*
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's response to the Restriction requirement filed on April 8, 2004 is acknowledged. Applicant's election of Group I, claims 1-21 without traverse is acknowledged. Applicant's election of species (c), SEQ ID NO:24 with traverse is acknowledged. Claims 22-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicant's traversal of the election of species in regards to Group I is acknowledged. The traversal is on the grounds that second species requirement is directed to Group II (claims 22-26) and not Group I (claims 1-21). Applicant urges that the species election in regards to the elected invention, Group I be removed. While it is true that the second species requirement is directed to Group II (claims 22-26) and not Group I (claims 1-21) which was due to a typographical error. The Office apologizes for the typographical error. However, SEQ ID NOs: 21, 22 and 24 (which are directed to the elected invention Group I, claims 1-21) are independent and distinct sequences based on structural differences. The election of species requirement made for these sequences was not in error. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 25. Applicant is asked to review the specification for hyperlinks and delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as a part of the invention an antibody or fragment thereof that binds to the *Bacillus anthracis* protective antigen. The specification discloses the claimed antibody or fragment thereof can include about 3 to 18 modifications. Applicant has broadly described the invention as embracing any substitution and deletion change of amino acids throughout the length of the amino acid sequence. The claims broadly encompass a genus of antibodies that bind the *Bacillus*

anthracis protective antigen. There is substantial variability among the species of antibodies that bind the *Bacillus anthracis* protective antigen encompassed within the scope of the claims. The specification does not place any structure limitations on the claimed antibodies. The scope of the claims include numerous structural variants and the genus is highly variant because a significant number of structural difference between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the compound class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. Since the claimed genus encompasses antibodies yet to be discovered, the mere recitation of a "antibodies or fragments thereof that bind immunologically to *Bacillus anthracis* protective antigen with an affinity K_d of between about 140 pM and about 21 pM as determined by surface plasmon resonance" does not provide an adequate written description of the claimed genus since no structure accompanies the function of binding to a *B. anthracis* protective antigen. While mutagenesis techniques are known in the art, it is not routine in the art to screen for multiple modifications within the amino acid's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining a certain activity or function are limited in any peptide.

Thomas E. Creighton, in his book, "Proteins: Structures and Molecular Properties, 1984", (pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes:

1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; 2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a Proline residue, which must distort the alpha-helix; 3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain- have no great effect on stability.

Thomas E. Creighton, in his book "Protein Structure: A Practical Approach, 1989; pages 184-186" teaches that present day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions". The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in "Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph) adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

One skilled in the art would not recognize from the claimed disclosure that the applicant was in possession of the genus of amino acid sequences that are required for the claimed invention. The recitation of "...binding affinity of between about 140 pM and about 21 pM as determined by surface plasmon resonance" does not convey a common structure. As such, generic amino acid sequences that are unrelated via structure are highly variant and not conveyed by way of the written description in the specification at

the time of filing. Therefore, the specification lacks written description for the highly variant genus of amino acid sequences that have the claimed function and one of skill in the would not recognize that Applicants had possession of the genus of the claimed antibodies as instantly claimed.

The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) The skilled artisan cannot envision the detailed chemical structure of the antibody or fragments thereof that are encompassed by the claimed invention regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Therefore, the claims do not meet the written description provision of 35 USC 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-21 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-21 recite "monovalent antibody portion". It is unclear as to what Applicant is referring? Clarification is required.

5. Claims 1-21 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-21 recite "between about". It is unclear as to what Applicant is referring? Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1, 4-8 and 18-21 are rejected under 35 U.S.C. 102(a) as anticipated by Maynard et al *(Nature Biotechnology, Volume 20, June 2002).*

Claims 1, 4-8 and 18-21 are drawn to an isolated antibody or fragment thereof that specifically bind immunologically to *Bacillus anthracis* protective antigen with an affinity K_d of between about 140pM and about 21 pM as determined by surface plasmon resonance.

Maynard et al teach an antibody, 1H scfv that has a K_d of 0.25 nM (250 pM) (Table 1, page 599) which is an isolated antibody that specifically bind immunologically to *Bacillus anthracis* protective antigen with an affinity K_d of between about 140 pM and about 21 pM as determined by surface plasmon resonance. Maynard et al teach that the antibody constructs were a molecular weight of about 45 kDa (page 598). The claim limitation "...further defined as comprising Fc domain of IgA, IgD, IgE, IgG or IgM" would be inherent in the teachings of the prior art. Maynard et al, anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's antibody with the antibody of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the antibody of the prior art does not possess the same material structural and functional characteristics of the claimed antibody). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

7. No claims are allowed.

Conclusion

8. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
June 17, 2004

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600